Abstract

Sub-Saharan Africa accounts for high tuberculosis cases that result from widespread HIV infections, which is exacerbated by injection substance use. Immunologically, HIV critically impairs cell-mediated host responses to Mycobacterium tuberculosis. IFN-γ, IL-10 and Acrp30 are key mediators of systemic inflammation. Although circulating IFN-□ and IL-10 levels are increased, Acrp30 levels are lowered and associated with disease severity among HIV and TB co-infected non-susbstance users. In contrast, circulating IFN-□ and Acrp30 levels are decreased while IL-10 levels are upregulated among injecting heroin addicts. However, no studies to date have reported on these cytokine profiles among Kenyan HIV-1 and TB co-infected injection drug users. This study, therefore, investigated plasma IFN-γ, IL-10 and Acrp30 levels among IDUs, and their association with CD4+ T cell counts, HIV-1 viral load and BMI. A cross-sectional study was conducted from August, 2012-November, 2013 using 138 participants recruited at Bomu hospital; a major centre for rehabilitation of drug and substance users in Mombasa County. Following informed consent, IDUs were enrolled through respondent driven sampling, snowball and makeshift methods while convenience and purposive sampling were used for recruiting the control group. IDUs and controls were screened for HIV and TB respectively through Determine™ and Bioline™ rapid tests, and Ziehl Neelsen stained sputum smears. Subsequently, the study participants were categorised into: HIV-1/TB coinfected ART-naive (n=9) and -experienced (n=27); HIV-1 mono-infected ARTnaive (n=26) and -experienced (n=13); TB mono-infected (n=21), HIV-1 negative and TB uninfected (n=25) IDUs and controls (n=17). Demographic, drug use information and physical measurements were recorded using assisted interviews. EDTA venous blood samples were collected and used for preparing plasma and enumerating CD4+ T cell counts. Frozen plasma samples were used for determining cytokine concentrations, and HIV-1 viral load. CD4+ T cell counts were enumerated using flow cytometry; cytokine levels were measured using a sandwich ELISA technique, while HIV-1 viral load was determined by RT-PCR, respectively. Across-group comparisons in continuous data were performed using Kruskal Wallis followed by post-hoc Dunn's tests. Plasma IFN-γ ($P<0.0001$), IL10 ($P<0.0001$) and Acrp30 ($P=0.006$) levels differed significantly across groups. IFN-γ levels were high in co-infected ART-naive ($P<0.001$) and -experienced ($P<0.001$), and HIV-1 mono-infected ART-experienced ($P<0.001$) IDUs relative to healthy controls. IL-10 levels were elevated in uninfected IDUs ($P<0.001$) compared to healthy controls. Acrp30 levels were lower in TB mono-infected ($P<0.01$)

relative to controls. IFN-γ/IL-10 ratio varied across-groups (P<0.0001) and higher in co-infected ART-naive (P<0.001) and -experienced (P<0.001), and HIV-1 mono-infected ART-experienced (P<0.001) compared to uninfected IDUs. The IFN-γ/Acrp30 ratio also differed across groups (P<0.0001) with HIV-1 mono-infected ART-experienced (P<0.001), and co-infected ART-naive (P<0.001) and -experienced (P<0.001) IDUs exhibiting higher ratio relative to uninfected IDUs. CD4+ T cells correlated inversely with Acrp30 (□=-0.717, P=0.030) levels in TB mono-infected IDUs whereas BMI correlated positively with Acrp30 (□=0.523, P=0.022) among co-infected ART-naive IDUs, respectively. Altogether, circulating IFN-□, IL-10 and Acrp30 production is altered in ART-naive and -experienced HIV-1 and TB co-infected IDUs, suggesting a role as disease markers in HIV and TB co-infection among IDUs.